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Special Article

What Analytical Chemists Do : A Personal Perspective*

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ABSTRACT

Analytical chemistry has played an important role in the development of civil societies and commerce throughout history. The perceived value of gold and silver probably was the first incentive to acquire analytical knowledge. Analytical chemists today play key roles in the function of modern societies, impacting nearly all aspects of our lives. Agricultural, clinical, environmental, forensic, manufacturing, and pharmaceutical testing are a few examples. Modern instrumentation gives analytical chemists incredible capabilities to measure complex mixtures for organic compounds and trace metals, with abilities for speciation and time and spatial resolution. Some of the tools we use and the information we can obtain from them are described as examples of what the profession of analytical chemistry is about.

Keywords: analytical chemistry, example tests, instrumentation, tools.

1. INTRODUCTION

The role of analytical chemistry dates from biblical times [1]. Why do we need analytical chemists? Analytical chemistry deals with the characterization of matter. Everything is made of chemicals, and we need chemical information about many substances and materials. Analytical chemists provide this for us.

So just what do we do? The late Charles N. Reilley at the University of North Carolina, in his Fisher Award address at the April 1965 ACS meeting, stated "Analytical chemistry is what analytical chemists do" [2]. There are more formal definitions of the discipline. One reasonable definition [3] is that analytical chemistry provides the methods and tools needed for insight into our material world for answering four basic questions about a material sample:

- What?
- Where?
- How much?
- What arrangement, structure or form?

The discipline consists of qualitative analysis (what?) and quantitative analysis (how much?) (Figure 1). From proper sampling and measurements, we can ascertain the variation with respect to position (where?) and determine the species present –chemical speciation (what arrangement, structure or form?). Very often we will have qualitative information (we know there is glucose in our blood), and we need quantitative information.

A workshop on Education in Analytical Chemistry was held in Cordoba, Spain in 2001, and the importance of analytical chemistry in our lives was highlighted [4]. It was pointed out that 5% of the Western World's economy is dependent on analysis, and 50% of chemists use analytical methods or results. There are some 5 billion pieces of analytical data generated per year in just the European Union. Dr. Manfred Grasserbaur from the Institute

*From Dr. Bruno Werdelmann Foundation Lecture, Chiang Mai, Thailand, February 1, 2005.

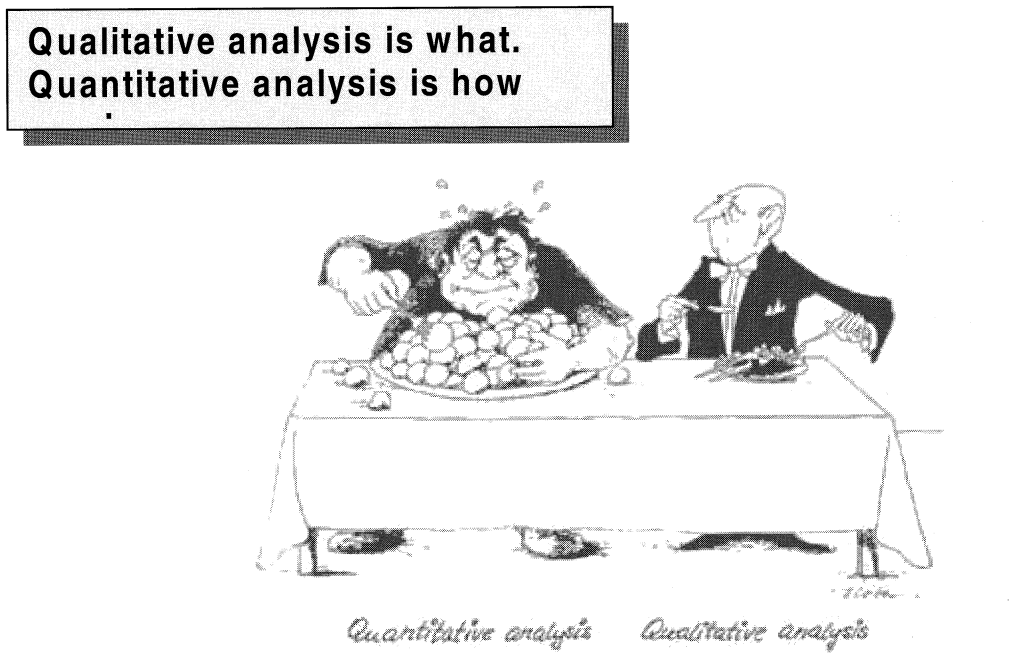

Figure 1. Qualitative and quantitative analysis.

for Reference Materials and Measurements in Belgium suggested that 60% of all legislation requires scientific input, and that analytical chemistry provides measurements leading to knowledge. Since knowledge is the basis of democratic governance, analytical chemistry is therefore indispensable to governing a modern society. A challenge for analytical chemists is to educate policy makers as to what their measurements represent. While legislation may be passed to effectively mandate zero concentration of a chemical effluent in water, zero being defined as non-detectable levels, our capabilities now are such that we can measure very low natural occurrences of chemicals or levels below which a chemical can reasonably or technologically be reduced. On the other hand, our measurements are very valuable in verifying compliance where appropriate.

2. Some Examples

The impact of analytical chemistry on our everyday lives can be illustrated with a few examples.

• *Blood glucose measurement.* This represents perhaps the largest number of analytical chemistry measurements in the world. When we have our annual physical checkups, our blood glucose level is measured to determine if we are at risk of becoming diabetic. Diabetic patients must monitor their blood glucose levels on a regular basis. There are numerous ways to perform this analysis. For home monitoring, there are several devices that allow automated readout from a pin-prick blood sample (Figure 2). These are based on a selective enzymatic reaction that converts the glucose to an equivalent amount of hydrogen peroxide, which is then measured electrochemically or from a color producing reaction.

There is research in progress to develop implantable sensors that will provide continuous monitoring of blood glucose levels and allow controlled release of insulin.

• *Cholesterol levels.* A common diagnostic aid is the measurement of blood cholesterol level, as a predictor of potential heart attack risk. We can distinguish between low density lipoprotein cholesterol (LDL – bad choles-

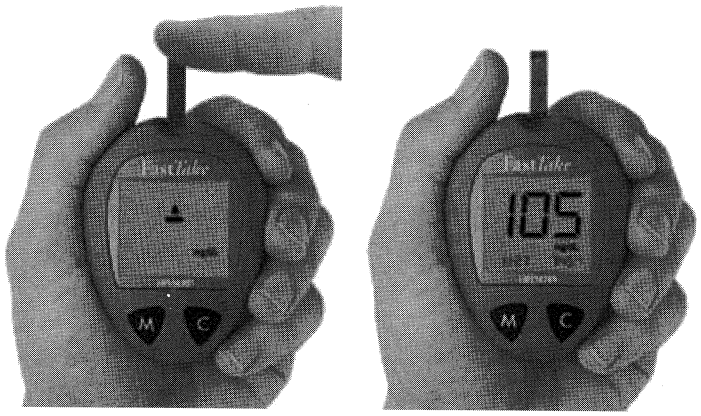

Figure 2. Blood glucose monitor. LifeScan *(www.lifescan.com)*.

terol) and high density lipoprotein cholesterol (HDL – good cholesterol).

• *Vitamin content of food.* We can assess the nutritional value of foods by chemical analysis.

• *Pesticides in foods.* We can identify contamination of foods by chemical analysis.

• *Carbon monoxide in air.* We can monitor atmospheric carbon monoxide, and warn of unhealthy levels. Carbon monoxide home monitors can detect when a defective furnace emits dangerous levels that may be fatal, and sound an alarm.

• *Auto emissions.* Many municipalities require annual measurement of carbon monoxide and hydrocarbon emissions from auto exhausts, and require repair of autos that are out of compliance. This done using an infrared sensor that is inserted in the tailpipe (the chemicals of interest absorb specific frequencies or wavelengths of infrared radiation).

• *Water hardness.* A measure of water quality is the amount of calcium and magnesium minerals, which can react with detergents or soaps and decrease their effectiveness. The water hardness, expressed as parts per million of calcium carbonate, is determined by reacting the calcium and magnesium ions with a complexing agent, EDTA (in a titration).

• *Nitrogen in fertilizer.* The quality of fertilizer and its price are determined by its content, as well as other constituents such as potassium.

• *Carbon in steel.* The carbon content of steel affects its strength. Other ingredients, such as manganese, are also important, and we can measure these by a variety of techniques.

• *Gunshot residue.* The presence of certain elements such as barium from gunpowder on a hand is an indication an individual has fired the weapon. Forensic analysis is really analytical chemistry in practice. DNA analysis is an important modern forensic tool.

• *Illicit drugs.* We can identify illicit street drugs, or identify the presence of forbidden performance-enhancing drugs like steroids in athletes. Usually a screening procedure is used, for example immunochemical analysis, to identify a class of drugs, and the presence of an actual drug is confirmed and identified by a very selective technique, gas chromatography-mass spectrometry (see below). This is the procedure followed at the Olympics. It is very difficult to escape the capability of the analytical chemist!

• *Rapid identification of toxic substances.* Analytical chemists are key in identifying suspected toxic substances that may put the public at risk.

• *Chemical warfare agents.* In this day of terrorism, analytical chemistry is essential to monitor for and detect chemical agents. There is much ongoing research to develop rapid field tests for specific agent detectors. When

your handbag is checked for explosives by airport security, the technique of ion mobility spectrometry is used, which can detect traces of nitrogen-containing explosives on a swab rubbed over your bag.

These are but a few examples of how analytical chemists improve and protect our lives. Analytical chemistry is important in:

- *Health* – prevention and detection of disease
- *Safety* – natural and manmade dangers, protection of our food supplies
- *The environment* – monitoring our air, water, and soil. There are new technologies that allow remote sensing, with transmission of data to a computer for analysis.
- *Manufacturing* – quality control (quality of products), improving manufacturing efficiency by providing real-time analyses of chemical intermediates or products and providing feedback control to optimize the chemical reaction. This improves economic competitiveness.
- *Regulations* – performing measurements to ensure compliance
- *Forensics* – obtain objective evidence in criminal cases

3. What Tools Do We Use?

The analytical chemist has a host of tools for obtaining analytical information, both qualitative and quantitative. Just a few examples will illustrate some of the more important ones and the incredible capabilities of the analyst.

- *The chemical balance (gravimetry).* The chemical balance is one of the oldest and most important tools for measurements. The balance received divine approval in the earliest documents found. Proverbs 11:1 states "A false balance is an abomination to the Lord, but just weight is his delight". The art and science of the balance was known in Egypt from about 3000 B.C. An example of a 2000 year old balance is shown in Figure 3, not exactly a microbalance, but nonetheless an important tool in commerce. Precision balances were developed in the 18th century by Henry Cavendish. The double pan balance (Figure 4), based on a first class lever, can measure milligram quantities of material. The sample is placed on one pan and is balanced by an equal mass on the other pan. Modern balances are electronic (Figure 5), but are still based on calibration against a known mass.

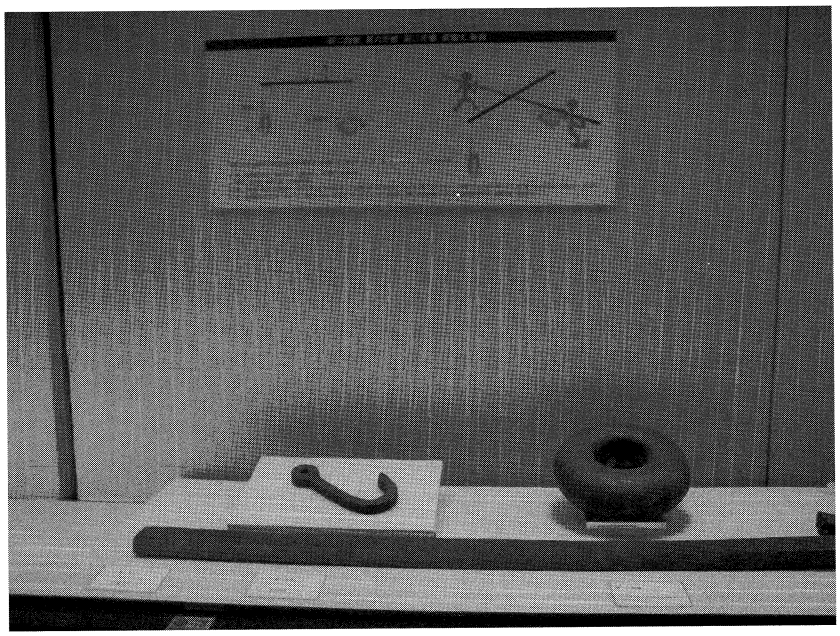

Figure 3. Balance from Han Dynasty, 10 A.D. *(Taiwan National Museum, Taepei).*

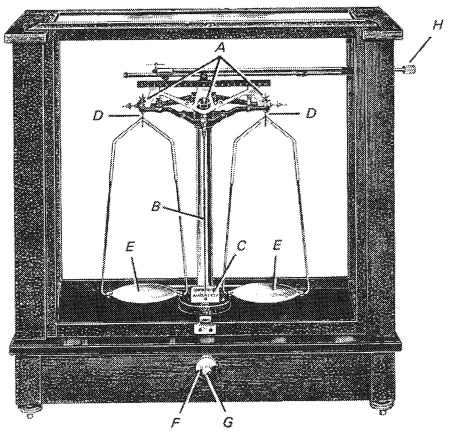

Figure 4. Double pan balance. *(G.D. Christian, Analytical Chemistry, 3rd ed., Wiley).*

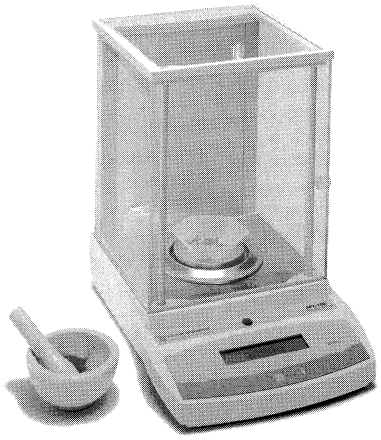

Figure 5. Electronic balance. *(G. D. Christian, Analytical Chemistry, 6th ed., Wiley).*

We can measure microgram quantities with some balances.

One of the most accurate and precise chemical analyses is gravimetry, in which the substance to be determined is precipitated by reaction with a reagent to form a known compound which is isolated and accurately weighed. For example, chloride ion in table salt (sodium chloride) can be reacted with silver ion to precipitate silver chloride. From the weight of silver chloride, and the known fraction of chloride in it, we can calculate the weight of chloride which came from the sample. This measurement is so accurate that it was used by T. W. Richards at Harvard University 100 years ago to determine atomic weights!

• *Volumetric glassware (titrimetry).* We must make accurate and precise measurements of solutions. Accurate volumetric glassware allows us to do this. A pipet (Figure 6) is used to obtain and deliver a fixed volume of solution, for example, 10.00 milliliters. A volumetric flask (Figure 6) is used to dilute a

Pipets Volumetric flask Buret

Figure 6. Volumetric glassware. *(G. D. Christian, Analytical Chemistry, 6th ed., Wiley).*

solution to a fixed volume, for example 100.0 milliliters, by filling to a marked line. A buret (Figure 6) is used to deliver variable volumes of solutions, measured accurately to 0.01 milliliter, e.g., 37.97 milliliters.

The technique of titrimetry is again one of the most accurate and precise measurement methods, and was developed in the 18th and 19th centuries. Here, the sample is reacted with a known concentration of a reagent (e.g., chloride ion is reacted with silver ion from a silver nitrate solution), delivered from a buret until the reaction is just complete, as noted by a chemical indicator that changes color at that point. From the concentration of silver nitrate and the volume delivered, we can calculate the number of moles (molecules) of silver reacted with the chloride, and this will equal the moles of chloride in the sample titrated.

• *Spectrophotometry.* Many substances are colored in solution or can be reacted with a reagent to form a colored derivative. A solution is colored because it absorbs certain wavelengths of the electromagnetic spectrum (light), and passes the complement color, which is the color we see. A blue solution, for example, absorbs the yellow colors. The more concentrated the solution, the more of the yellow radiation is absorbed, and the darker blue the solution, i.e., the amount of absorbed yellow wavelengths is proportional to the concentration of the absorbing species. If we can measure that, we have a measure of the concentration.

If white light is passed through a prism, it is diffracted and spread into the spectrum wavelengths or colors of the rainbow. Suppose we place a slit at the position of the yellow radiation, blocking the others. We can then pass only the yellow radiation through our blue solution, and measure the amount absorbed. This forms the basis of the technique of spectrophotometry.

The light source can be a tungsten bulb, like the light in an auto headlight. The intensity of the selected wavelength passing through the solution is measured with a photocell or photomultiplier tube. The photoelectric effect causes electrons to be emitted from a photoemissive surface to generate a current, which we measure. (Albert Einstein explained the photoelectric effect in 1905 and received the Nobel Prize in Physics in 1922 for this – not for the theory of relativity!).

A very accurate spectrophotometer was invented by Arnold Beckman, introduced by Beckman Instruments Company in 1941 (Figure 7). It was developed because of the need to measure vitamin A in food.

We can also obtain qualitative information from spectrophotometric measurements. We can rotate the prism or grating that disperses the radiation so that different wavelengths pass the slit and get absorbed by the sample (this scanning can be done automatically). Each wavelength is absorbed to a different degree by a given

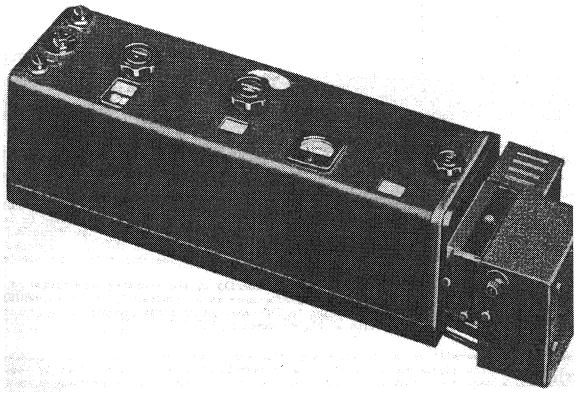

Figure 7. Beckman DU spectrophotometer introduced in 1941 *(Alan J. Bard, Pittcon, 2002).*

substance, creating a fingerprint of the amount absorbed as a function of wavelength, which may be unique to that substance.

Spectrophotometry is the most widely used analytical chemistry technique. It is not restricted to the visible region, and measurements in the ultraviolet and the infrared regions are very useful. The latter, in particular, can provide very specific spectral fingerprints for qualitative identification (recall the auto exhaust measurements).

• *Flow injection analysis.* In spectrophotometric analysis, we need to add known volumes of reagents (with pipets), dilute to a known volume (in a volumetric flask), and transfer to a cuvet for measurement in the spectrophotometer. These operations can be eliminated by injecting a small volume, only microliters, of sample solution into a flowing stream of reagent. The sample and reagent mix as they flow, react, produce a color, and the plug of colored product flows through a spectrophotometer flow cell to give a transient signal, the magnitude of which is a measure of the sample concentration. This operation requires only a few seconds, and generates very small amounts of chemical waste. Any spectrophotometric procedure can be adapted to the technique of flow injection analysis (FIA). A compact instrument is shown in Figure 8. Microdevices such as lab-on-chip are useful for diagnostic testing and for field testing of chemical and toxic agents, such as chemical warfare agents.

The International Conference on Flow Injection Analysis (ICFIA) is held every two years, and was hosted in 2001 by Chiang Mai University Department of Chemistry, where leading research on FIA is performed [5]. Professor Kate Grudpan at Chiang Mai University has been a pioneer in developing simple and inexpensive FIA equipment, and the introduction of microfluidics and lab-at-valve technologies. For this and other work, he was recognized as the "Outstanding Scientist of the Year in Thailand" in 2001, and a "Thailand Outstanding Person in Science and Technology" in 2004.

• *pH meter.* pH is a measure of acidity or basicity of a solution (a neutral solution has pH 7, an acidic one less than 7, and an alkaline (basic) one more than 7). pH measurements are important in many aspects of chemistry, and in determining properties of samples. There are various means of measuring pH, but the most widely used is the pH meter, using an electrode whose electrical potential is responsive to the hydrogen ion. Arnold Beckman introduced the first pH meter in 1936 (Figure 9), and formed the Beckman Instruments Company, which became a very successful manufacturer of analytical chemistry

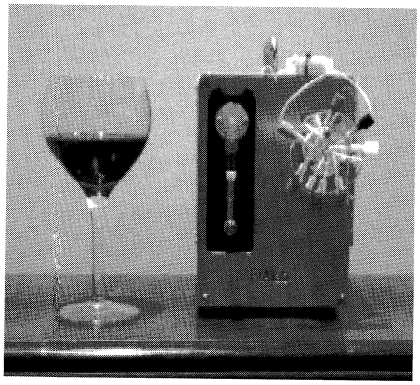

Figure 8. Flow injection analyzer *(FIA lab Instruments: www.flowinjection.com).*

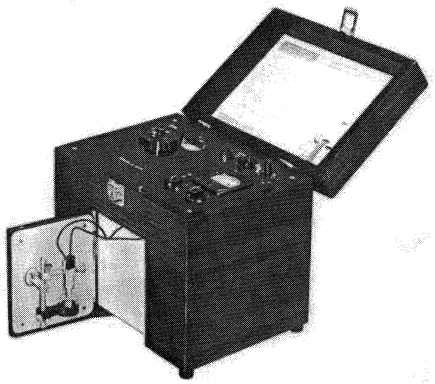

Figure 9. Beckman Model G pH meter, introduced in 1936 *(http://chem.ch.huji.ac.il/~eugenik.instruments/electrochemical/bp_meter_beckman_g.html).*

instruments. He developed the "acidimeter" at the request of a friend in the citrus industry who needed to measure the acidity of lemons.

• *Gas chromatography.* A very powerful tool for analyzing complex mixtures is gas chromatography. A modern gas chromatograph is shown in Figure 10, including an autosampler for automatic introduction of samples. Suppose we inject a tiny amount of gasoline sample into a heated oven at the top of a column (chromatography column) whose surface contains chemical groups that can interact with compounds that come in contact with it. The volatile constituents in the gasoline are vaporized. We flush the gaseous molecules down the column with an inert gas like helium. The many compounds will each interact differently with the column and move down the column at different rates. We detect them as they emerge from the end of the column to record a gas chromatogram (Figure 11). We see that the resolving power for this complex mixture is great. Different components of the sample are identified from the times at which they appear, by comparison with times for elution of standards of known compounds, and their peak heights or areas are measures of the amounts.

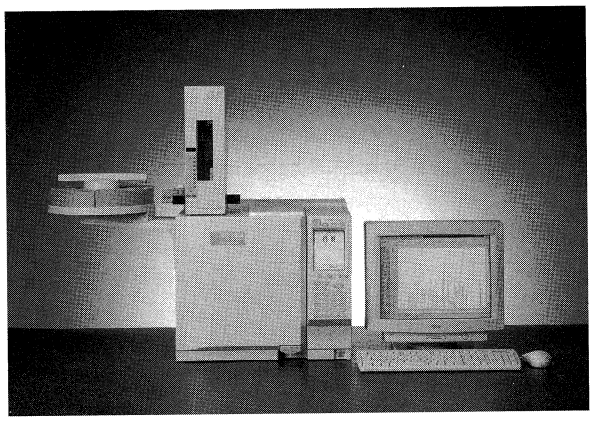

Figure 10. Modern gas chromatograph system *(G.D. Christian, Analytical Chemistry, 6th ed., Wiley).*

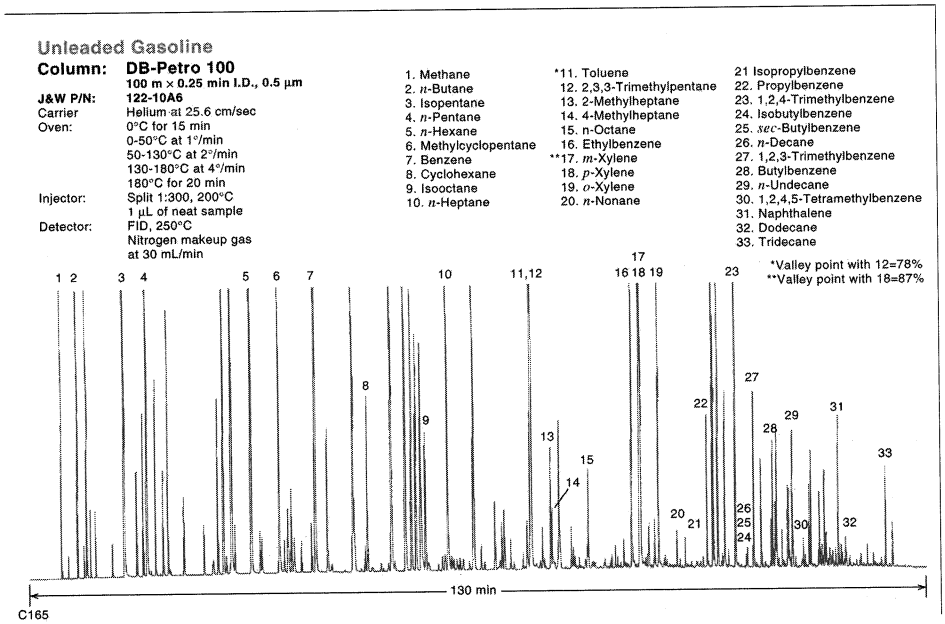

Figure 11. Typical gas chromatogram of complex mixture *(G. D. Christian, Analytical Chemistry, 6th ed., Wiley).*

Many substances can be volatilized or reacted with a reagent to form a volatile derivative, and so this is a very widely used technique. It is used to measure the blood alcohol content in suspected drunk drivers, for example when there is an injury or death (the GC measurement of blood is more accurate than a breath test for court purposes). There are a variety of very sensitive GC detectors. The ultimate is a mass spectrometer. In this instrument, the molecules are bombarded with electrons, which causes the molecules to fragment and to become charged. This creates a molecular fingerprint of the molecule, and may even give its molecular weight. Figure 12 shows the chromatogram of a suspected cocaine sample at the top. The peak at 11.6 minutes is

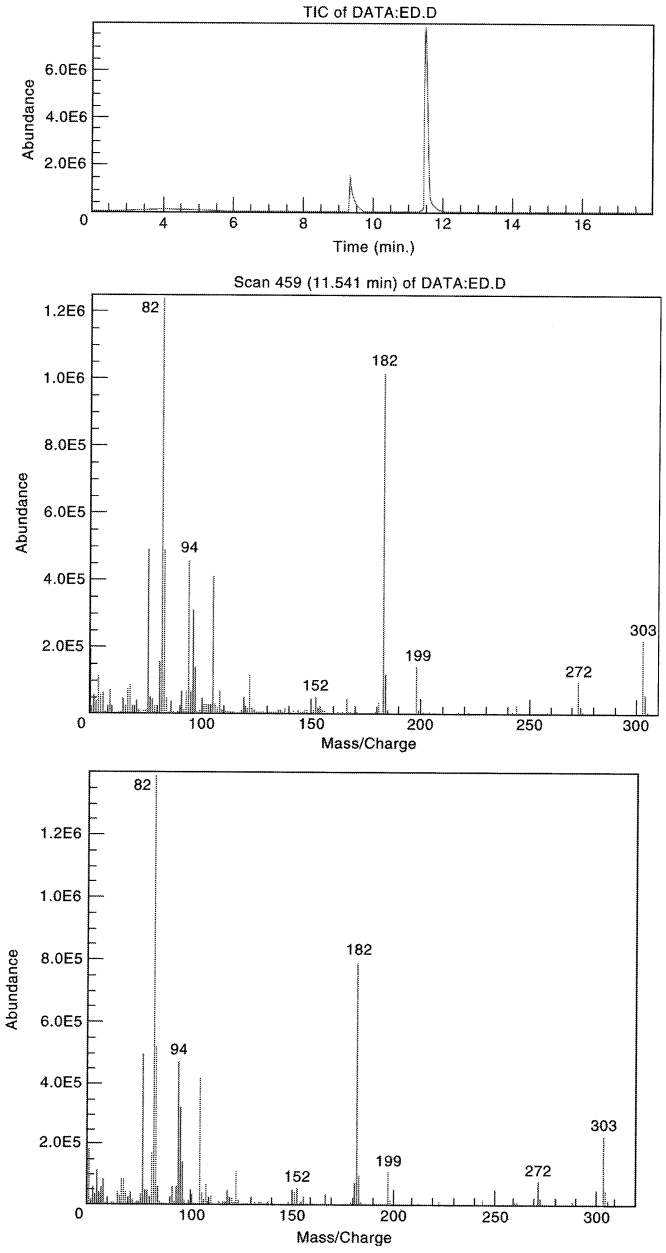

Figure 12. Confirmation of cocaine by GC-MS *(G.D. Christian, Analytical Chemistry, 6th ed., Wiley).*

indicative of cocaine. The mass spectrum for that peak is shown in the middle, which is identical to that of cocaine shown at the bottom, positively confirming this is a cocaine sample. This technique of gas chromatography-mass spectrometry (GC-MS) is a very powerful way to confirm beyond reasonable doubt what the eluting molecule is – this is how we keep Olympic athletes honest.

There are other forms of chromatography that also allow analysis of liquid samples, and the principles are the same.

• *Gel electrophoresis – genomics.* Our cells contain 23 pairs of chromosomes, composed of DNA (deoxyribonucleic acid) - the double helix, which determines our genetic makeup (Figure 13). The double helix is held together by the pairing of four nucleic acid bases, guanine (G), thymine (T), cytosine C, and adenine (A). An A always pairs with a T, and a G always pairs with a C. It is the sequence of these bases that determines our genetic code, and there are some 3 billion base pairs that comprise the entire genetic code in the human genome. The Human Genome Project identified all 3 billion pairs, and put them in proper sequence. Analytical chemistry measurements did this [6].

The story is complex, but in essence, the long DNA strand was broken into small pieces of about 300,000 bases. These were magnified many fold by a procedure called the polymerase chain reaction (PCR). These individual fragments were then further randomly degraded to give every possible length (one base removed from the end at a time). The end base on each random fragment is tagged with a fluorophore molecule, and each of the four bases exhibits a different fluorescent color.

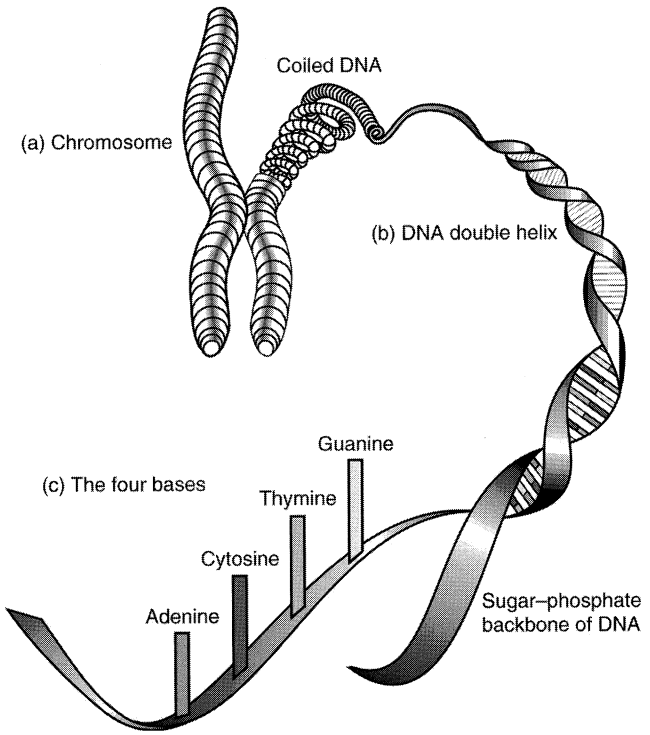

Figure 13. Chromosome structure. Each chromosome consists of tightly coiled double stranded DNA, which when uncoiled reveals double-helix structure *(G. D. Christian, Analytical Chemistry, 6th ed., Wiley).*

Now the fragments (nucleotides) of different lengths are separated based on size, using the technique of gel chromatography. In Figure 14, each spot in a column or lane represents an increase of one base in the chain length (each column is a different sample). So we know which base is at the end of each chain fragment, and hence we know the sequence of bases in the entire chain. We repeat this process for other DNA fragments, line up the overlapping portions, and then we have sequenced the entire human genome!

The PCR reaction is used in forensics to multiply traces of DNA for sequencing to positively identify an individual from which it came (each person has a unique sequence).

• *Polyacrylamide gel electrophoresis–proteomics.* The ultimate roles of genes are to code for the production of proteins, which perform most life functions. In order to learn about how disorders create disease, we need to know what protein a given DNA encodes (there are about 30,000 genes that code for proteins).

The science of protein identification, structure, and protein interactions is called *proteomics*. It is a much more daunting task than sequencing the genome. The technique of two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) separates proteins, first based on charge, and then based on size. The result is a powerful separation tool (Figure 15).

Suppose the dark spot at the bottom of the plate is a protein that appears only in a certain disease. We can extract that spot, degrade the protein into fragments of peptides (made up of amino acids), and then identify these by mass spectrometry. There are large databases of some 100,000 proteins that allow identification of the protein from the amino acid sequence. If we can identify the gene that encodes that protein, then we may be able to devise a drug or other treatment for the disease. Proteomics forms the basis of much drug discovery research.

• *Atomic force microscopy.* We can even look at individual atoms to study material properties and to learn more about our chemical world. The technique of atomic force microscopy (AFM) is based on a tiny cantilever with a nanometer sized tip that can be scanned over a surface. Atomic forces dictate the movement of the cantilever. Its small motion is detected by reflecting a laser beam off it to a motion sensitive detector (Figure 16). Figure 17 shows individual atoms on a nickel surface. Such surface measurements are critical in studying and understanding catalysts, which are very important in many chemical industries,

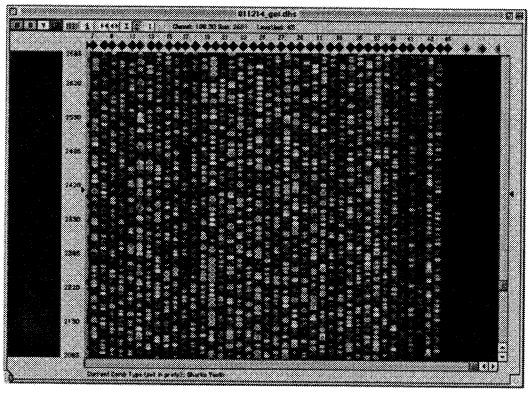

Figure 14. Gel electrophoresis of nucleotides. Each vertical lane represents a different sample. Bases are separated in order of size. Each band in a lane has one of the four base colors *(G. D. Christian, Analytical Chemistry, 6th ed., Wiley).*

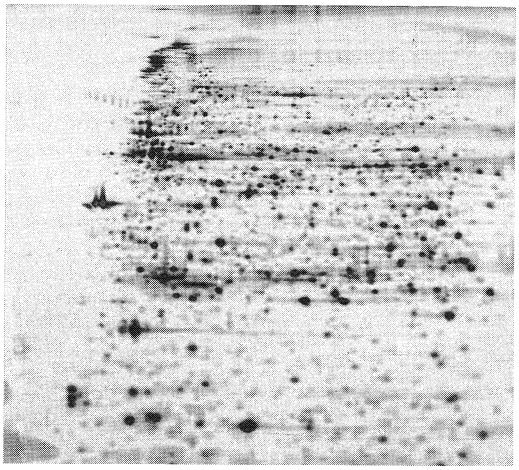

Figure 15. 2-D gel separation of proteins *(G. D. Christian, Analytical Chemistry, 6th ed., Wiley).*

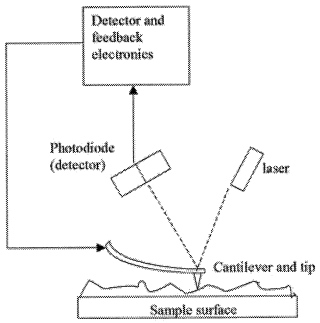

Figure 16. Atomic force microscope *(http://en.wikipedia.org/wiki/Atomic_force_microscope).*

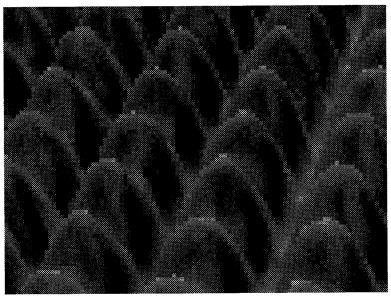

Figure 17. AFM picture of nickel atoms. IBM tunneling microscope image *(gallery - http://www.almaden.ibm.com/vis/stm/blue/html).*

to improve the efficiencies of chemical reactions. Catalysts in your automobile help reduce hydrocarbon emissions.

These are but a few examples of the tools that analytical chemists use to perform routine as well as very complex analyses. Many more examples may be cited, but this introduction has hopefully given the reader an appreciation of the importance of analytical chemistry and what analytical chemists do.

There are still many challenges ahead, and our capabilities will continue to improve, through research and identification of problems that need solving. To quote Professor Alan J. Bard of the University of Texas at Austin, "While we analytical chemists share an interesting and quite amazing history, the best is yet to come" [7]. And as Lord Kelvin said, "Unless our knowledge is measured in numbers, it does not amount to much".

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